Sexually Transmitted Infections

Editorials

South Africa: host to a new and emerging HIV epidemic

Southern Africa is experiencing a rapidly growing HIV epidemic, and this small region currently accounts for a disproportionately large segment of the global burden of new HIV infections.[1] In this region, HIV is spreading predominantly through heterosexual contact and clade C is the predominant subtype. In 1996, the reported HIV prevalence among antenatal clinic attenders from the southern African countries of Zimbabwe, Malawi, and Botswana were 40%, 30%, and 30% respectively.[2]

Before 1987 HIV infection in South Africa was rare.[3] Annual, anonymous, national HIV seroprevalence surveys conducted among first time antenatal clinic attenders provide an indication of the emergence and trends in the progression of HIV infection in South Africa. In the past 10 years HIV seroprevalence has risen from 0.76% in 1990 to 10.44% in 1995 to 22.8% in 1998,[4] with no signs of having reached a plateau. It is estimated that there are currently 3.5 million South Africans infected with HIV. This rapidly growing HIV epidemic in South Africa is best described as explosive.

An HIV incidence of 11.9% in 1997 in women between the ages of 15 and 30 years derived from repeat antenatal seroprevalence surveys (each with a sample size of approximately 1000) conducted in Hlabisa, a rural community on the east coast of South Africa, from 1992 to 1997, illustrates the explosive nature of the HIV epidemic.[5] Even in the relatively low incidence year of 1993, 3.8% of HIV negative women became infected. Young women in the general population in South Africa are experiencing HIV infection rates previously seen only in high risk sex worker populations.[6 7] HIV is spreading most rapidly in young women in South Africa; HIV prevalence grew from 6.9% in 1992 to 21.1% in 1995 in the 20–24 year old age group,[8] highlighting the importance of youth in the South African HIV epidemic.

Community based, HIV seroprevalence surveys conducted in one rural area of South Africa in 1990 and 1992 demonstrated that HIV infection was four times more prevalent among women (1.6%) than men (0.4%) and that women become infected at an earlier age than men.[9] A repeat survey in 1994 demonstrated a 2.3-fold sex difference in HIV prevalence, showing a narrowing of the sex gap as the epidemic progresses.[10]

Migrant labour is a major factor in the spread of HIV and other sexually transmitted diseases in South Africa. Despite the demise of apartheid, migration is still part of the reality of many South African lives. A woman's risk of HIV infection is substantially increased if her partner is a migrant worker. A study from rural South Africa found that women whose partners spent 10 or fewer nights per month at home had an HIV prevalence of 13.7% compared with 0% in women who spent more than 10 nights in a month with their partners.[10] Using crude measurements of mobility/migration, population based surveys from rural KwaZulu-Natal found about 2.5 times more infections among mobile adults compared with adults resident in the area continuously for more than a year.[9] Among women, migration was associated with an age adjusted 2.4-fold higher risk of HIV infection compared with a 7.3-fold higher risk among men.[9] The patterns of migration and sexual networking are fairly complex and implications for the spread of HIV and other sexually transmitted diseases are elaborated further in a paper by Lurie *et al.*[11]

The associated epidemic of sexually transmitted infections (STIs) is also a major contributor to the burden of disease in South Africa. On any given day about one in every four of the approximately 60 000 women aged 15–49 years in Hlabisa is infected with at least one STI.[12] Of these, 48% are asymptomatic, 50% are symptomatic but not seeking care, and only 2% seek care during an illness episode. Of these handful of women who seek care, only two out of three women are adequately treated for the STI.[12] A policy of syndromic management of STIs as well as the integration of STI services into the general primary healthcare services, adopted in 1995, have been steps in the right direction in terms of managing the huge burden of STIs; however, its success at the health facilities level has been impeded by poor drug supplies, low condom use, inability to encourage partner referral for treatment, and the social stigma associated with seeking STI treatment.

The most common HIV/AIDS presenting opportunistic infection in South Africa is tuberculosis. The progression from asymptomatic HIV to early disease is best reflected in the rise in new tuberculosis cases and the number of co-infections with HIV. New tuberculosis cases have a similar age and sex profile to that seen in the HIV epidemic. In Hlabisa, co-infection with HIV in adult tuberculosis rose from 36% in 1993 to 59% in 1995 and 65% in 1997.[13]

What makes the South African HIV epidemic a new and emerging explosive epidemic? Compared with other countries in eastern and central Africa, HIV infection in South Africa is a new phenomenon. Despite the late introduction of the virus it has been experiencing an intensely rapid growth and progression of the HIV epidemic. Having already reached high levels of infection there is no indication of stabilisation or plateauing of the epidemic. The migrant labour system and high levels of other sexually transmitted diseases are factors that are enhancing the transmission of HIV and fuelling this explosive epidemic. Of concern is the high HIV incidence rates in young people, and young women in particular.

The relatively late introduction of HIV into South Africa provided an opportunity to establish prevention programmes at an early stage. However, this opportunity was lost through the inability and lack of credibility of the previous government to institute any meaningful interventions. The new, democratically elected government while committed to addressing the HIV epidemic has to date also been unable to mount a response of the scale and magnitude required to turn this epidemic around. The current state of the HIV epidemic in South Africa poses many challenges. The continued and explosively rapid spread of HIV can be reduced through strategic and decisive action. Significantly, and in the medium to long term, how to reduce the impact of migration on HIV transmission and improve the status of women in the face of a bleak economic future and current high unemployment rates are urgent questions. While the focus must continue to be on preventing new HIV infections, strategies to deal with the increasing burden of HIV related diseases and AIDS as well as the impact of the premature loss of lives must also be developed. The success of these strategies will depend on the ability to develop effective partnerships between government, civil society, private and non-governmental sectors.

Q ABDOOL KARIM
Centre for Epidemiological Research in South Africa, South African Medical Research Council and Southern African Fogarty HIV/AIDS International Training and Research Programme, South Africa

S S ABDOOL KARIM
Centre for Epidemiological Research in South Africa, South African Medical Research Council, South Africa and Division of Epidemiology, Columbia University, New York, USA

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The use of HIV resistance assays—random or randomised?

High frequency error prone replication is the mechanism by which HIV-1 exhibits Darwinian evolution of its reverse transcriptase and protease genes in a changing drug environment and which may be one of the causes of treatment failure.[1] Genotypic and phenotypic resistance assays have been developed to evaluate this evolution of drug resistant virus and many clinicians and virologists consider that there is sufficient research based knowledge to introduce these assays into the routine clinical care of individuals with HIV-1 infection.[2] This process will take time and access is likely to be inequitable at the outset, depending largely on the response of fund holders to requests for funding. Purchasers will rightly be reluctant to provide resources for health interventions until there is evidence of their clinical value and, increasingly, their cost effectiveness. How strong is this evidence at present for HIV resistance testing?

In vitro, HIV-1 grown in the presence of one or more antiretroviral drugs will rapidly evolve mutations that are associated with loss of sensitivity to the drug.[3] In vivo, early studies showed that loss of virological suppression with monotherapies was associated with evolution of genotypic and phenotypic resistance.[4] Retrospective analysis of stored specimens of subgroups of patients in clinical trials suggested that resistance at baseline or evolving during therapy was associated with clinical failure.[5 6]

The rationale for resistance testing is to optimise therapy, particularly when drugs are being changed following virological failure. Instead of changing all components of a regimen, resistance testing should allow continuation of drugs to which the virus is still sensitive, thereby preserving a wider range of therapeutic options for the future. However, a number of important factors underlie this simple hypothesis.[1]

(1) Although several studies have demonstrated a strong association between the presence of certain mutations and phenotypic drug resistance,[7] our knowledge of the association is incomplete and will always remain so, particularly when drugs are used in combination as they are now. In addition, the link between resistance, particularly genotypic, and therapeutic failure is less clearly established for some drug classes.[8]

(2) The interpretation of genotypic resistance results is highly complex, particularly when drugs are used in combination as they are now. More research is needed to develop and validate algorithms to interpret results, which will be an integral part of clinical guidelines, and on the best way to deliver advice to clinicians. However, it is unlikely that resistance tests will ever be able to predict in vivo activity of individual drugs with complete accuracy.

(3) Current genotypic and phenotypic assays both have their limitations in a clinical setting: they require 1000–2000 HIV-1 RNA copies per ml of plasma from specimens collected from patients while on drug therapy to measure resistance reliably and are unable to detect minority species. High throughput phenotypic assays are expensive and are only performed in specialist units (none in the United Kingdom).

(4) Treatment failure is not always the result of resistance; other important factors include non-adherence, individual pharmacokinetics, and drug interactions.

Information on the predictive value of genotypic and/or phenotypic results for the selection of new regimens in patients who are failing therapy is very limited. Two small prospective randomised controlled trials have explored the use of resistance assays in highly treatment experienced individuals failing therapy and provide some evidence to support its use.[9 10] The VIRADAPT and CPCRA 046